REMARKS

A copy of a February 26, 2003 Associate Power of Attorney in the instant application that was granted to Kevin J. McGough by an attorney of record for the Applicants is attached herewith. Authorization is hereby given, and the Patent and Trademark Office is hereby requested, to charge Biogen Deposit Account 02-2327 for all fees required in connection with the filing of the instant Response. If, for whatever reason, the Patent and Trademark Office will not charge those fees to Biogen Deposit Account 02-2327, authorization is hereby given to charge the fees in the alternative to Coleman, Sudol & Sapone Deposit Account 04-0838.

Applicants respectfully request that future communications in connection with the instant application be addressed to Mr. McGough care of Coleman, Sudol & Sapone at the address provided below. Mr. McGough's office phone number is 914-337-4082.

Claims 1-21 are pending in this application. Claims 8, 9, and 11-21 were withdrawn from consideration on May 21, 2002, solely in response to the restriction requirement imposed in the Office Action dated March 22, 2002. Applicants have expressly reserved the right to prosecute the nonelected claims in another application. Claims 1-4, 6, 7, and 10 have been finally rejected and are hereby cancelled. Claim 5 has been allowed. Proposed new claims 22-39 are presented herein for the Examiner's consideration, in accordance with 37 C.F.R. § 1.116.

Applicants' understand that the format of the claim amendments presented in this Response conforms to the February 25, 2003 United States Patent and Trademark Office proposed revisions to 37 C.F.R.§ 1.121. Applicants' undersigned counsel respectfully requests that the Examiner inform him immediately by telephone if that is not the case in order that Applicants may submit a reformatted Response that conforms to the proposed revisions.

The Examiner has withdrawn the objections to the specification imposed in the July 30, 2002 Office Action.

Applicants maintain that the instant amendments comply with 37 C.F.R. § 1.116 and present new claims 22-39 that are either in a condition for allowance as they address

all of the outstanding grounds for rejection or, in the alternative, constitute amended versions of pending claims that are in a better condition for appeal. MPEP 714.13. Proposed new claims 22-39 address each of the Examiner's grounds for rejection of cancelled claims 1-4, 6-7, and 10, do not raise issues of new matter, and do not present new issues requiring further consideration or search. *Id.* Applicants respectfully request that the Examiner provide a prompt confirmation that new claims 22-39 have been entered and are allowable.

Claim Rejections: 35 U.S.C. § 112

The Examiner has maintained her rejections of claims 1-3 and 10 under 35 U.S.C.§ 112, ¶ 1, on grounds that the specification, while being enabled for TGF-β RII/Fc fusion proteins of SEQ ID NOS: 8 and 9, allegedly reasonably does not provide enablement for all TGF-β R fusion proteins. Per the Examiner, claims 1-3 and 10 were nonenabled because they were not limited to molecules of defined homology to TGF-β RII (e.g., claims 1 and 10), were not limited with respect to the definition of the claim term "TGF-β receptor" (e.g., claims 1 and 10), or, even where limited to type II receptors, were not limited to TGF-β RII (claims 2 and 3). In the interests of expediting prosecution, claims 1-3 and 10 have been cancelled and proposed new claims 22-39 are presented for the Examiner's consideration. Claims 22-39 address each of the Examiner's grounds for rejecting claims 1-3 and 10 under Section 112, ¶ 1.

For example, proposed new independent claims 22 and 27 claim TGF-β RII fusion proteins comprising: (1) a biologically active amino acid sequence which corresponds to all or all part of the extracellular region of native TGF-β RII and which is at least 60% homologous to SEQ ID NOs: 8 or 9 or equivalents thereof or naturally occurring variants thereto; and (2) a constant region of an immunoglobulin, wherein the fusion protein binds to TGF-β. Thus, the proposed new claims obviate any conceivable enablement issue of the type raised by the Examiner.

Support for each of the proposed new claims 22-39 is found throughout the specification as originally filed, e.g., at page 26, lines 15-31, at page 27, lines 1-17, at page 28, lines 4-13, and in each of the Examples.

Claim Rejections: 35 U.S.C. § 103

It is respectfully submitted that proposed new claims 22-39 also address all of the bases for the Examiner's rejection of cancelled claims 1-4, 6, 7, and 10 under 35 U.S.C. § 103(a) ("Section 103(a)") as being unpatentable as obvious in light of U.S. Patent No. 6,046,157 ("*Lin*") in view of U.S. Patent No. 5,605,690 ("*Jacobs*"). While Applicants do not concede that *Lin* and *Jacobs*, whether taken individually or in combination, disclose or in any way suggest fusion proteins or pharmaceutical compositions of any of the pending claims, those references certainly do not disclose or in any way suggest fusion proteins or pharmaceutical compositions within the scope of proposed new claims 22-39. The limitations recited in new independent claims 22, 27, 30, and 35 with respect to the components and sequences of the claimed fusion proteins are not found in, or in any way suggested by, the prior art.

The Examiner has still not provided the requisite rigorous showing of a clear and particular suggestion, teaching, or motivation to combine *Lin* and *Jacobs* to yield the claimed TGF-β RII/Fc fusion proteins. *In Re Dembiczak,* 50 U.S.P.Q.2d 1614 (Fed. Cir. 1999). It is impermissible hindsight to combine these two references in the absence of such a rigorous suggestion, teaching, or motivation. *Id.*

As noted in the Response to the July 30, 2003 Office Action, the Examiner has admitted that *Lin* does not teach Fc fusion proteins and that *Jacobs* does not teach TGF-βRII fusion proteins (the reference describes fusion proteins for soluble TNFα receptors). *Lin's* disclosure at column 7, lines 63-67- column 8, lines 1-7, that TGF- β II and III receptors can be used as both agonists and antagonists to alter the effect of TGF- β *in vivo* is not a clear and particular suggestion of the fusion proteins and pharmaceutical compositions of proposed new claims 22-39. *Lin's* observation at column 9, lines 54-58, that there appear to be correlations between levels of TGF- β production and certain diseases would not in any way motivate one of ordinary skill in the art to make fusion proteins and pharmaceutical compositions of proposed new claims 22-39. Speculating that modulation of TGF- β might have an ameliorative effect on certain diseases does not equate with a disclosure of fusion proteins and compositions of proposed new claims 22-

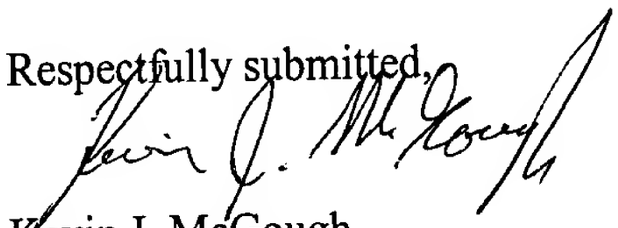
39: *Lin* does not even focus on TGF- β IIR, much less suggest that fusion proteins and related pharmaceutical compositions as defined by proposed new claims 22-39 would be useful in the treatment of a fibroproliferative disorder.

Jacobs's disclosure that chimeric, polyvalent forms of TNFR could have enhanced binding affinity for a TNF ligand would not have motivated one of ordinary skill in the art to make Applicants' wholly different type of fusion proteins. There is no support for the notion that because *Jacobs's* TNF chimeric antibodies were polyvalent, one of ordinary skill in the art would have: (1) decided to select TGF-β RII as a target for inhibition based on the unspecified TGF-β R disclosure of *Lin* (2) recognized that TGF-β RII/Fc fusion proteins, as defined by proposed new claims 22-39, could be used in the treatment of a fibroproliferative disorder, and (3) thereafter made TGF-β RII/Fc fusion proteins and pharmaceutical compositions as specified in proposed new claims 22-39. At best, *Lin* and *Jacobs* skirt around the production of fusion proteins and pharmaceutical compositions such as those of proposed new claims 22-39 and merely generalize about the properties of the TGF-β receptor class. Such disparate disclosures cannot be modified and cobbled together to render the claimed inventions obvious. *Hybritech Inc. v. Monoclonoal Antibodies, Inc.*, 231 U.S.P.Q. 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).

There is no basis to conclude that those of ordinary skill in the art would have used *Jacobs* as a template to select TGF-β RII from *Lin* in an effort to make the fusion proteins and pharmaceutical compositions of proposed new claims 22-39. Further, there would not have been any reasonable expectation that such a combination or modification would have proved successful. *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Not only was there no motivation in the art to select, modify, and combine *Lin* and *Jacobs* as suggested, there is no reason to believe that any advantages attendant to polyvalent TNF would translate to TGF-β RII fusion proteins and pharmaceutical compositions defined by proposed new claims 22-39.

In light of all of the foregoing, it is respectfully maintained that proposed new claims 22-39 should be entered and found to allowable together with allowed claim 5. It is respectfully maintained that each of those claims should be passed to issue.

Respectfully submitted,



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